FDA/ ASCO/AACR
Public Workshop on Clinical Trial Endpoints in Ovarian Cancer

April 26, 2006
Bethesda North Marriott Hotel and Conference Center
North Bethesda, Maryland

Background Information

History and Goals of Cancer Drug Approval Endpoints Project

The Public Workshop on Clinical Trial Endpoints in Ovarian Cancer is one of a series of FDA workshops evaluating potential endpoints for cancer drug approvals in the most common tumor types. Previous workshops have considered general issues related to trial endpoints as well as endpoints in lung, colorectal, and prostate cancer, acute leukemia, and primary brain tumors. Summaries and presentations from these earlier workshops are posted on FDA's Web site for the Project on Cancer Drug Approval Endpoints (http://www.fda.gov/cder/drug/cancer_endpoints/).

Issues highlighted at these workshops are subsequently discussed at meetings of the Oncology Drugs Advisory Committee (ODAC), the FDA's statutory advisory body on issues related to oncology drugs. Discussions both at the workshops and at ODAC will inform guidance that FDA is writing on clinical endpoints for cancer drug approvals.

The American Society of Clinical Oncology (ASCO) is providing logistical support for this workshop in conjunction with the American Association for Cancer Research (AACR).

Workshop Purpose

The purpose of the Public Workshop on Clinical Trial Endpoints in Ovarian Cancer is to engage in a thorough discussion of the pros and cons of a variety of endpoints for trials intended to support the approval of new drugs to treat ovarian cancer. The goal is to work toward the establishment of a set of principles on current and future standards of efficacy for these drugs. The primary focus will be on endpoints that are ready for incorporation into clinical trials now or in the near future. Workshop participants may identify key issues and areas in which knowledge is limited and may recommend issues or questions for further study. However, it is not the workshop panel's task to make recommendations or arrive at definitive conclusions. By law, FDA may take advice only from its statutory advisory committees.

Workshop Scope

The workshop's scope is limited to treatment of Stage III and Stage IV ovarian cancer.

Workshop Structure

The workshop will consist of formal presentations examining different types of clinical trial endpoints for drug approvals in ovarian cancer, interspersed with panel discussion. During

discussion periods, panelists will address specific questions posed by the FDA that focus on issues such as the accuracy, reproducibility, and clinical relevance of the various endpoints about which data have been presented.

Audience Participation

The workshop agenda will include several opportunities for members of the audience to make comments and ask questions of the panel. Members of the audience are asked not to interrupt speaker presentations or panel discussion but to hold their comments and questions until the designated audience question periods.

Workshop Agenda

Regulatory Background

Dr. Lee Pai-Scherf, FDA, will provide context for questions posed to the panel by reviewing regulatory terms and principles, as well as types of endpoints that have been used to approve cancer drugs, including agents currently approved for the treatment of ovarian cancer.

Clinical Trial Design Issues in Ovarian Cancer

Dr. J. Tate Thigpen of the University of Mississippi School of Medicine, co-chair of the panel, will discuss issues relating to the design of clinical trials for therapies in ovarian cancer, including the unique features of ovarian cancer that must be taken into account when designing trials.

Regulatory Use of CA-125 for Progression Evaluation in Ovarian Cancer

Dr. Robert C. Bast of the M.D. Anderson Cancer Center will discuss criteria that have been proposed for the use of CA-125 as a surrogate marker for response and disease progression. Dr. Gordon Rustin, Mount Vernon Hospital (United Kingdom), will discuss the use of CA-125 as an endpoint in both first-line therapy and relapsed disease and the use of rising CA-125 levels to assess drug activity in asymptomatic patients. Dr. Robert Becker, FDA, will offer the agency's perspective on analytical aspects of CA-125 tests.

Regulatory Endpoints for First-Line Therapy in Ovarian Cancer

Dr. Elizabeth Eisenhauer of the National Cancer Institute of Canada Clinical Trials Group, Dr. Mark F. Brady of the Gynecologic Oncology Group Statistical and Data Center, and Dr. Marc Buyse of the National Cancer Institute in Paris, France, will present data on the use of progression-free survival (PFS) as a surrogate for overall survival (OS) in first-line therapy and will discuss the pros and cons using PFS as an endpoint for clinical trials of first-line therapies.

Regulatory Endpoints for Maintenance Therapy in Ovarian Cancer

Dr. Robert F. Ozols of Fox Chase Cancer Center and Dr. David R. Spriggs of Memorial Sloan-Kettering Cancer Center will present data on the use of PFS and OS as endpoints in clinical trials of maintenance therapy for ovarian cancer and will discuss the pros and cons of the use of PFS as an endpoint for clinical trials of maintenance therapies.

Regulatory Endpoints for Subsequent Therapies in Ovarian Cancer

Dr. David R. Spriggs of Memorial Sloan-Kettering Cancer Center will discuss endpoints for clinical trials of therapies to treat recurrent ovarian cancer that is sensitive to platinum-containing agents. Dr. Peter G. Rose of the Cleveland Clinic Foundation will discuss endpoints for trials of therapies to treat platinum-resistant recurrent ovarian cancer.

Patient-Reported Outcomes in Ovarian Cancer

Dr. Lari Wenzel of the University of California–Irvine and Dr. Karen Basen-Engquist of the M.D. Anderson Cancer Center will discuss the use of patient-reported outcomes (PROs) in trials of therapies for ovarian cancer, identify PRO measures that are ready for incorporation into trials now, and highlight issues related to the use of PROs in ovarian cancer trials that require further study.

Biomarker and Endpoint Research Priorities

Dr. Edward G. Trimble, National Cancer Institute, will chair a session focusing on priorities for further research and development of biomarkers and other endpoints in ovarian cancer.

Workshop Summary/Conclusions

Dr. Stacy R. Nerenstone, Oncology Associates, and Dr. Ralph S. Freedman, M.D. Anderson Cancer Center, will summarize the panel discussion and outline the key points made during the workshop.

References

FDA Guidance Documents

Guidance for Industry – Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics. Draft Guidance. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). April 2005. http://www.fda.gov/cder/guidance/6592dft.pdf

Guidance for Industry – Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Draft Guidance. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research

(CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH). February 2006. http://www.fda.gov/cder/guidance/5460dft.pdf

3rd International Ovarian Cancer Consensus Conference - September 2004

Du Bois A, Quinn M, Thigpen T, Vermorken JB (guest editors). 3rd International Ovarian Cancer Consensus of the Gynecologic Cancer Intergroup (GCIG). Annals of Oncology 2005 (September), Vol. 16, Supp. 8. http://ctep.cancer.gov/resources/gcig/guest.pdf

Du Bois A, Quinn M, Thigpen T, et al. 2004 consensus statements on the management of ovarian cancer: final document of the 3rd International GCIG Ovarian Cancer Consensus Conference. Annals of Oncology 2005 (September), Vol. 16, Supp. 8. http://ctep.cancer.gov/resources/gcig/dubois.pdf

Quinn M, Avall-Lundqvist E, du Bois A, et al. History, scope and methodology of the 3rd International Consensus Workshop on Ovarian Cancer 2004. Annals of Oncology 2005 (September), Vol. 16, Supp. 8. http://ctep.cancer.gov/resources/gcig/quinn2.pdf

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Stuart G, Avall-Lundqvist E, du Bois A, et al. 3rd International Ovarian Cancer Consensus Conference: Outstanding issues for future consideration. Annals of Oncology 2005 (September), Vol. 16, Supp. 8. http://ctep.cancer.gov/resources/gcig/stuart.pdf

Thigpen T, Stuart G, du Bois A, et al. Clinical trials in ovarian carcinoma: Requirements for standard approaches and regimens. Annals of Oncology 2005 (September), Vol. 16, Supp. 8. http://ctep.cancer.gov/resources/gcig/thigpen.pdf

Vermorken JB, Avall-Lundqvist E, Pfisterer J, Bacon M. The Gynecologic Cancer Intergroup (GCIG): History and current status. Annals of Oncology 2005 (September), Vol. 16, Supp. 8. http://ctep.cancer.gov/resources/gcig/vermorken2.pdf

Vermorken JB, Parmar MKB, Brady MF, et al. Clinical trials in ovarian carcinoma: Study methodology. Annals of Oncology 2005 (September), Vol. 16, Supp. 8. http://ctep.cancer.gov/resources/gcig/vermorken1.pdf

Other Literature

Rustin GJS, Marples M, Nelstrop AE, et al. Use of CA-125 to define progression of ovarian cancer in patients with persistently elevated levels. J Clin Oncol 2001; 19: 4054-4057.